World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 6.129

A STUDY ON DRUG-DRUG INTERACTIONS DUE TO POLYPHARMACY IN TERITARY CARE HOSPITAL IN SOUTHERN INDIA

Lakshmi Meghana Potluri*, Mohana Mudhitha Vadlapatla, Jyothirmayee Kongara, Dhanush Bellapu, Padmalatha Kantamneni

Department of Pharmacy Practice, Vijaya Institute of Pharmaceutical sciences for Women, Enikepadu, Vijayawada, Andhra Pradesh, India.

***Corresponding Author: Lakshmi Meghana Potluri**

Department of Pharmacy Practice, Vijaya Institute of Pharmaceutical sciences for Women, Enikepadu, Vijayawada, Andhra Pradesh, India.

Article Received on 05/02/2020 **Article Revised on 26/02/2020** **Article Accepted on 16/03/2020**

ABSTRACT

The study was conducted to monitor the clinically significant complexity occur due to the use of multiple drug therapy which may further lead to drug drug interactions (DDI'S). Drug interaction generally refers to a modification of the expected drug response in the patient as a result of exposure of the patient to another drug or substance. DDIs became the commonest problem globally the overall DDIs which had occurred has been reported and recorded. The clinical outcomes may increase the risk of drug toxicity or increase adverse drug report (ADR). DDIs are divided into three groups depending on the underlying mechanism of interaction: pharmaceutical, pharmacokinetic, pharmacodynamic interactions. Polypharmacy is considered as one of the major risk factors in precipitation of DDIs. Patient population at high risk include the elderly and patients with co-morbidities as they are usually prescribed with more number of drugs. Critical evaluation of such prescriptions by pharmacist could result in identification and reduction of such problems.

KEYWORDS: Drug-Drug Interactions, Polypharmacy, Co-morbidities, Adverse Drug Reactions.

INTRODUCTION

A Drug-Drug Interactions(DDIs) is said to occur when the effects of one drug are changed by the presence of another drug or when two or more medications are simultaneously administered and medication increase or decrease the effectiveness of another.[2] Drug Interactions are classified into two types:

Pharmacokinetic Drug Interactions – One drug effects the Absorption; Distribution; Metabolism; Excretion of other drug.[6]

Pharmacodynamic Drug Interactions – Two or more drugs may have additive or antagonistic effect.[6]

Drug interactions may occur due to factors like age, polypharmacy, multiple prescribers and co-morbidities. These DDIs events shows a serious health complications to the patient and also increases the patient expenses.[1]

Drug therapy becomes more complex with polypharmacy. Prescriptions need to be evaluated thoroughly in order to avoid any changes of drug related problems.[6] Concomitant use of multiple drugs has been defined as polypharmacy. Polypharmacy often results in heightened risk of drug related problems. DDIs pose significant challenge to health care providers and may affect morbidity, mortality, and patients quality of life.[3]

The pharmacist along with the prescriber must ensure that the patients are aware of the side effects caused by the drugs. The rate of pharmacist is to promote drug utilization evaluation to minimize the drug interactions. The nature and severity of all DDIs should be identified to educate the physicians, nurses, staff etc.[4]

MATERIALS AND METHODS

Seven research articles are taken which were published in different journals. Those studies were held in different places of India. The methodology of the studies were shown in table -1.

Table 1: List of studies with the details of author, year of publication, study design, study period, study site, sample size, data base used.

Study	Author	Year	Study design	Study period	Study site	Sample size	Data base
1.	Javed Akhtar Ansari	2018	Prospective observational study	6 months	General medicine	100	Micromedex-2.0
2.	Siraj Sundaran	2018	Prospective Observational Study.	6 months	Department of Medicine	150	Micromedex, Drug-Drug interaction checker
3.	Akshay Khandeparkar	2017	Prospective cross-sectional observational study.	12 months	Department of medicine	5424	Lexi-com version 2.4.1.
4.	S. Priya Rajam Vivenan	2017	Prospective study	9 months	Department Of Medicine	50	Micromedex
5.	Gavini Siva Bharat	2016	Prospective observational study	6 months	General medicine department	100	Stockley's Medscape And BNF
6.	Akram Ahmad	2015	Prospective observational study	6 months	Medicinal department	404	Micromedex
7.	Nimmy N.John	2012	Prospective Observational study	6 months	Department of Medicine	200	Micromedex

RESULTS AND DISCUSSION

STUDY-1

A total of 100 cases were reviewed, with the age group between 18 to 75 years. A total of 87 prescriptions were found to have drug interactions. A total of 49 drug interactions were reported to the physician during the study period. Majority (22.8%, n=114) of the 10 interactions were moderate. Out of the total DDI identified, 27.9% were pharmacodynamic interactions and (60.3%) were pharmacokinetic interactions and (8.04%) interactions The Prevalence of drug interactions was 29.3%. The interactions found most frequently in the present study are ceftriaxone and furosemide (21.98%), followed by norfloxacin and ondansetron (13.7%), phenytoin and atorvastatin(11.4%), chlorpheniramine and midazolam (8.04%), azithromycin and calcium carbonate (2.29%) and enalapril and furosemide (1.14%). The results of our study revealed that the majority of drug interactions were found in the prescriptions of cardiovascular diseases. The least number of DDIs was observed in CNS related diseases (3.44%). While the prevalence of DDIs in prescriptions with respiratory disease, GI problems, endocrine diseases, and infectious diseases were 25.2%, 16.9%, 3.4%, and 5.74% respectively.[1]

STUDY-2

A total of 150 patient prescriptions were randomly collected among which 123 (82%) prescriptions were found with 396 DDIs. There were 65 (52.85%) males and 58 (47.15%) females. Among the 123 cases, 69 (56.1%) patients were in the age above 60 years followed by 38 (30.89%) patients within 46–60 years, 11 (8.94%) patients within age group of 31–45 years, and 5 (4.07%) patients within age group of range 18–30 years. The study found that there was a higher prevalence of DDIs among the patients above the age of 60 years (56.09%).Out of 396 DDIs, there were 90 (22.73%) pharmacokinetic DDIs and 306 (77.27%) pharmacodynamic DDIs. The different pharmacokinetic DDIs, where drug interactions due to altered metabolism were found most often 48 (53.33%) followed by absorption-related drug interactions 22 (24.44%), interactions-related excretion 16 (17.77%), and altered distribution 4 (4.44%). Pharmacodynamic DDIs had synergistic drug interactions 209 (68.30%) and antagonistic drug interactions 97 (31.69%). Among the DDIs, there were 324 (81.81%) moderate DDIs followed by 42 (10.61%) major DDIs and 30 (7.58%) minor DDIs. out of 396 DDIs, 380 (95.96%) were unintentionally prescribed and 16 (4.04%) were intentionally Prescribed. Among the DDIs observed majority of interactions, 127 (32.07%) could be managed by monitoring signs and symptoms followed by dose adjustment 48 (12.12%). Among 123 prescriptions, 32 (26.01%) DDIs occurred in Neurology Department, 25 (20.32%) in Cardiology Department, 14 (11.38%) in Endocrinology Department, 14 (11.38%) in Pulmonology Department, 12 (9.75%) in Infectious Department, 9 (7.31%) in Gastroenterology Department 9 (7.31%) in Urology Department, 4 (3.25%) in Dermatology Department, and 4 (3.25%) in Hematology Department.[2]

STUDY-3

A total of 5424 prescriptions were collected from the three departments and analyzed during the study period.751 prescriptions out of 5424 (13.85%) prescriptions were observed to have polypharmacy with highest rates observed in the Department of Medicine. The median age of patients was 55.60 ± 13.86 (range, 10–108 years). Four hundred and seventy-six patients were male (63.4%) and 275 (36.6%) were females. Percentage of elderly patients (age 60 or more) was 41.5% as compared to 58.5% of patients with age <60

years. Total number of drugs per prescription ranged from minimum of 5 to maximum of 16 drugs, with an average of 7.96 ± 1.75. Five hundred and ninety-six prescriptions contained 6–9 drugs per prescription. More than ten drugs per prescriptions were observed in 79 prescriptions. Potential for DDIs was present in 706 out of 751 (94%) prescriptions with polypharmacy. A minimum of one potential DDI to a maximum 25 potential DDIs could be identified in a single prescription in the 706 prescriptions. Most of the prescriptions (*n* = 205) had 5–7 harmful DDIs. Out of 706 prescriptions with DDIs, 79 prescriptions had more than ten drugs, followed by 323 prescriptions with 8–10 drugs and 304 prescriptions with 5–7 drugs. Sixteen out of 706 (2.3%) prescriptions had at least one DDI classifiable as "X" (combination should be contraindicated), whereas 415 prescriptions had at least one DDI of "D" type where drug therapy should be modified and 688 prescriptions had at least one DDI classifiable as "C" where drug therapy has to be monitored. A prospective, observational study from the cardiology department in a hospital from South India reported an incidence of 30.67% of potential DDIs.[3]

STUDY-4

Out of selected 50 patients,6 patients (12%) were in the age group of 20-30 years, 2 patients (4%) were in the age group of 30-40 years, 12 patients (24%) were in the age group of 40-50 years, 10 patients (20%) in the age group of 50-60 years, 10 patients (20%) in the age group of 60-70 years, 8 patients (16%) in the age group of 70-80 years of age and 2 patients (4%) in the age group of 80-90 years of age. The mean age of the patients was 55.4 years. 50 prescriptions were analyzed out of which 34 (68%) were male and 16 (32%) were female. Among them 2 prescriptions were with major interactions, 52 prescriptions with moderate and 12 prescriptions with minor interactions. Majority of the patients were in the age group of 55-60 years. Among them 9 patients (18%) were having Diabetes, 5 patients (10%) were having Hypertension, 8 patients (16%) were having Bronchial Asthma, 6 patients (12%) were having lower respiratory tract infection, 20 patients (40%). From them 76% are of pharmacokinetic and 22% are of pharmacodynamic interactions. Average number of drugs per prescription (12.55) indicates the incidence of polypharmacy, and in most cases it was unavoidable.[4]

STUDY-5

In our study, 100 prescriptions were screened within a study period of 06 months. Based on gender distribution there were 65 prescriptions of male and 35 of female prescriptions. In our study, we compared three international drug interactions compendia to assess the severity of drug - drug interactions. The drug interactions appendix of British National Formulary (BNF). BNF uses a bullet to mark interactions that are potentially hazardous and where combined administration of the drugs involved should be avoided. The Stockley's Drug Interactions is used to précis the mass of literature into a concise and easy-to-read form, the text has been organized into a series of individual monographs, all with a common format. To inform busy healthcare professionals, of the facts about drug interactions, without their having to do the time-consuming literature searches and full assessment of the papers for themselves, Clinical Pharmacology Database Medscape Database. According to Stockley's drug interactions: Each monograph has been assigned a rating symbol to offer guidance to the user on the clinical significance of the interaction. These ratings are the same as those used in Stockley's Interaction Alerts. The Alerts are rated using three separate categories: *action, severity and evidence.* These ratings are combined to produce one of four symbols. For interactions that have a life-threatening outcome, or where concurrent use is contraindicated by the manufacturers. **(X)** For interactions where concurrent use may result in a significant hazard to the patient and so dosage adjustment or close monitoring is needed**.(!)** For interactions where there is some doubt about the outcome of concurrent use, and therefore it may be necessary to give patients some guidance about possible adverse effects, and/or consider some monitoring. **(?)** For interactions that are not considered to be of clinical significance, or where no interaction occurs. **(√)**. In these study, 14 was identified as significant hazard to the patient, 9 was identified as possible adverse effects, 3 was identified as non-clinical significance.[5]

STUDY-6

A total of 404 patient's case records were reviewed in general medicine ward during six months study period in which 214 (53%) patients were males and 190 (47%) patients were females. The mean age of patients was (48±17.93) ranging from 18 to 95 y. Out of 404 case records reviewed, 139 (34.4%) DDIs were identified and 78 (19.3%) patients had pDDIs. The number of drugs was ranging from 3 to 10 drugs (Mean+ SD: 6±2.13). Majority (54%) of the patients presented enrolled in this had some kind of past medical problems. The study shows that most frequent drug interaction was between paracetamol and pantoprazole 25 (17.98%), followed by ofloxacinondansetron 21 (15.1%) theophylline-budesonide 19 (13.66%), ibuprofen-ofloxacin 9 (6.47%), Mefenamic acid-atenolol/amlodipine 12 (8.63%), frusemide-aspirin 9(6.4%). The study also highlighted on the severity of pDDIs and found that majority of 75 (53.95%) pDDIs were moderate in nature, 44 (31.65%) were found to be severe and 20 (14.38%) were found to be mild. This study revealed that the prevalence of pDDIs were higher in pain/fever prescriptions (25.1%). Conversely, least number of pDDIs was observed in arthritis patients (2.1%). While the prevalence of pDDIs in prescriptions with respiratory disease, cardiovascular disease, GI problems, Diabetic issues and skin reactions were 17.9%, 15.8%, 12.9%, 15.1% and 3.5% respectively.[6]

STUDY-7

A total of 117 prescriptions (58.5%) were found to have drug interactions in 200 prescriptions. Out of which 78(66.6%) were male and 39(33.3%) were female patients. Out of 117 drug interactions, 85 (72.6%) were reported from Out Patient department and remaining 32 (27.3%) were from In patient department. Age was found to be an important criteria in the fact that the patients in the age group 51-70 years has experienced maximum DIs (61.5%) followed by 23% in the age group 41-50 years. Out of 117 interactions, 38 were from pulmonary department, 34 from Gastroenterology department 29 from Cardiology department and 14 from Neurology department. Severity of the drug interactions was observed. Among that 20.1% were minor, 66.2% were moderate and 13.63% were severe interactions.[7]

CONCLUSION

Our study was designed to assess the DDIs that occur in hospitalized patients in tertiary care hospital. The medication chart of in-patients were collected and checked for drug interactions. The main cause of drug interactions was polypharmacy, co-morbid conditions and elderly were found to be associated with more number of DDIs. The DDI are checked in computarized software data bases like - Micromedex, Stockely's, DDI Checker by using these softwares the severity of DDIs were estimated. Majority of DDIs are Pharmacokinetic in nature hence periodic auditing of prescription is vital for promoting rational use of drugs increases therapeutic efficacy and minimizing drug interactions. The first step in managing drug interactions is to be aware of patients taking potentially interacting drugs. The clinicians and health care professionals at the study site require an awareness program on DDIs and their management in improving the clinical outcomes.

ACKNOWLEDGEMENT

The authors are thankful to Vijaya Institute of Pharmaceutical Sciences for Women, Enikepadu, Vijayawada for valuable support and guidance.

CONFLICT OF INTEREST

We have no conflict of interest.

REFERENCES

1. Rahila Tarannum, Arifa Muneeb, A prospective observational study on drug-drug interactions in department of general medicine at a tertiary care hospital, International Journal of Advances in Pharmacy Medicine and Bioallied Sciences, 2018; 6(2): 53-58.
2. S. Priya Rajam Vivean, M. Ashok Kumar and P. Shanmugasundaram, Prospective study on drug-drug interactions of narrow therapeutic index drugs, IJPSR, 2017; 8(12): 5303-5307.
3. Gavini Siva Bharat, Maddineni Nagarjuna, Uppara Veerendra, Dr. Mohanraj Rathinavelu Mudhaliar, Narayana Goruntla, A study on severity of drug interactions and their inclusion in various drug information compendia, ejpmr, 2016; 3(7): 376-380.
4. Akram Ahmad, Muhammad Umair Khan, Irfanul Haque, Rahul Ivan, Ram Dasari, Megha Revanker, A. Pravina, Sheetal Kuriakose, Evaluation of Potential Drug - Drug Interactions in General Medicine Ward of Teaching Hospital in Southern India, Journal of Clinical and Diagnostic Research, 2015 Feb; 9(2): 10-13.
5. Nimmy N. John, R.H. Udupi and K.M. Binu, incidence of polypharmacy induced drug interaction in a tertiary care hospital, IJPSR, 2012; 3(7): 2119-2121.
6. Greeshma K George, Siraj Sundaran, Ashar Ali Cp, Mubeena Km, Thansiya Ph, Babu G, Arun Gopalakrishnan, Study of Drug-Drug Interaction in the inpatients of a Tertiary Care Hospital at Calicut, Asian J Pharm Clin Res, 2018; 11(9): 162-164.
7. Akshay Khandeparkar, Padmanabh V. Rataboli, A study of harmful drug–drug interactions due to polypharmacy in hospitalized patients in Goa Medical College, http://www.picronline.org on Tuesday, February 25, IP: 117.246.218.163, 2020.
8. Baxter K, Stockley's drug interactions, General Considerations and an Outline Survey of Some Basic Interaction Mechanisms, 7th ed. London: Pharmaceutical Press, 2006; 1.
9. Bushardt RL, Massey EB, Simpson TW, Ariail JC, Simpson KN, Polypharmacy: Misleading, but manageable, Clin Interv Aging, 2008; 3: 383-9.
10. Alomar MJ, Factors affecting the development of adverse drug reactions, Saudi Pharm J, 2014; 22: 83-94.